WHAT IS CLAIM IS:

1. At least one compound of the formula (I):

$$R_{20} \xrightarrow{R_6} \xrightarrow{M} \xrightarrow{R_2} \xrightarrow{Z} Z_1$$

$$Q \xrightarrow{R_3} \xrightarrow{R_7} \xrightarrow{R_5} \xrightarrow{R_1} Z_1$$

$$Q \xrightarrow{R_1} \xrightarrow{R_2} \xrightarrow{Z} Z_1$$

$$Q \xrightarrow{R_3} \xrightarrow{R_7} \xrightarrow{R_7} X_1$$

$$Q \xrightarrow{R_1} \xrightarrow{R_2} \xrightarrow{R_3} X_1$$

$$Q \xrightarrow{R_1} \xrightarrow{R_2} \xrightarrow{R_1} X_2$$

$$Q \xrightarrow{R_1} \xrightarrow{R_2} \xrightarrow{R_2} X_1$$

$$Q \xrightarrow{R_1} \xrightarrow{R_2} \xrightarrow{R_2} X_2$$

$$Q \xrightarrow{R_1} \xrightarrow{R_2} \xrightarrow{R_2} X_1$$

$$Q \xrightarrow{R_1} \xrightarrow{R_2} \xrightarrow{R_2} X_2$$

$$Q \xrightarrow{R_1} \xrightarrow{R_2} \xrightarrow{R_2} X_1$$

$$Q \xrightarrow{R_1} \xrightarrow{R_2} \xrightarrow{R_2} X_2$$

wherein

M is O or S;

R₁ is H, F, an alkyl group, OH, SH, or an O-alkyl group;

R₂ and R₅ are independently selected from H,

$$X$$
 Y_1
 A_1
 B_1
 D_1
 A_2
 A_2

or an alkyl group, wherein said alkyl group is different from

$$X$$
 Y_1
 A_1
 D_1
 A_2
 D_2
 D_2
 A_2
 D_2

with the proviso that at least one of R2 or R5 must be

$$X$$
 Y_1
 A_1
 B_1
 D_1
 Or
 X
 Y_2
 A_2
 A_2
 D_2
,

and wherein, when R2 or R5 is

$$X^{Y_{l}}$$
 A_{l}
 D_{l}

X is =CH or =CF and Y₁ is =CH or =CF,

or X and Y₁ together with Q' form a three-membered ring in which Q' is -C(R₁₀)(R₁₁)- or -O-, X is -CH- or -CF-, and Y₁ is -CH-, -CF-, or -C(alkyl)-, where R₁₀ and R₁₁ independently are H, a halogen, or an alkyl group, or, together with the carbon atom to which they are attached, form a cycloalkyl group or a heterocycloalkyl group,

or $X \text{ is -CH}_{2}$ -, -CF₂-, -CHF-, or -S-, and $Y_1 \text{ is -O-, -S-, -NR}_{12}$ -, -C(R₁₃)(R₁₄)-, -C(O)-, -C(S)-, or -C(CR₁₃R₁₄)-,

wherein R₁₂ is H or alkyl, and R₁₃ and R₁₄ independently are H, F, or an alkyl group, or, together with the atoms to which they are bonded, form a cycloalkyl group or a heterocycloalkyl group;

A₁ is C, CH, CF, S, P, Se, N, NR₁₅, S(O), Se(O), P-OR₁₅, or P-NR₁₅R₁₆, wherein R₁₅ and R₁₆ independently are an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group, or, together with the atom to which they are bonded, form a heterocycloalkyl group;

 D_1 is a moiety with a lone pair of electrons capable of forming a hydrogen bond; and

 B_1 is H, F, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, $-OR_{17}$, $-SR_{17}$, $-NR_{17}R_{18}$, $-NR_{19}NR_{17}R_{18}$, or $-NR_{17}OR_{18}$,

wherein R_{17} , R_{18} , and R_{19} independently are H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, or an acyl group;

and with the provisos that when D_1 is the moiety $\equiv N$ with a lone pair of electrons capable of forming a hydrogen bond, B_1 does not exist; and when A_1 is an sp^3 carbon, B_1 is not $-NR_{17}R_{18}$ when D_1 is the moiety $-NR_{25}R_{26}$ with a lone pair of electrons capable of forming a hydrogen bond, wherein R_{25} and R_{26} are independently H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group;

and wherein D_1 - A_1 - B_1 optionally forms a nitro group where A_1 is N; and further wherein, when R_2 or R_5 is

$$X^{Y_2}$$
 A_2
 B_2
 D_2

X is =CH or =CF and Y_2 is =C, =CH, or =CF,

or X and Y₂ together with Q' form a three-membered ring in which Q' is -C(R₁₀)(R₁₁)- or -O-, X is -CH- or -CF-, and Y₂ is -CH-, -CF-, or -C(alkyl)-, where R₁₀ and R₁₁ independently are H, a halogen, or an alkyl group, or, together with the carbon atom to which they are attached, form a cycloalkyl group or a heterocycloalkyl group,

or X is -CH₂-, -CF₂-, -CHF-, or -S-, and Y₂ is -O-, -S-, -N(R'₁₂)-, -C(O)-, -C(R'₁₃)(R'₁₄)-, -C(S)-, or -C(CR'₁₃R'₁₄)-,

wherein R'₁₂ is H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, - OR'₁₃, -NR'₁₃R'₁₄, -C(O)-R'₁₃, -SO₂R'₁₃, or -C(S)R'₁₃, and R'₁₃ and R'₁₄, independently are H, F, or an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group, or, together with the atom to which they

are attached, form a cycloalkyl group or a heterocycloalkyl group;

A₂ is C, CH, CF, S, P, Se, N, NR₁₅, S(O), Se(O), P-OR₁₅, or P-NR₁₅R₁₆, wherein R₁₅ and R₁₆ independently are an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group, or, together with the atom to which they are bonded, form a heterocycloalkyl group;

D₂ is a moiety with a lone pair of electrons capable of forming a hydrogen bond; and

 B_2 is H, F, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, $-OR_{17}$, $-SR_{17}$, $-NR_{17}R_{18}$, $-NR_{19}NR_{17}R_{18}$, or $-NR_{17}OR_{18}$,

wherein R_{17} , R_{18} , and R_{19} independently are H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, or an acyl group;

and further wherein any combination of Y_2 , A_2 , B_2 , and D_2 optionally can form a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group;

 R_3 and R_6 are independently H, F, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, -C(O) R_{17} , -OR₁₇, -SR₁₇, -NR₁₇R₁₈, -NR₁₉NR₁₇R₁₈, or -NR₁₇OR₁₈,

wherein R₁₇, R₁₈, and R₁₉ independently are H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, or an acyl group;

or, R₃ and R₆, together with the carbon atom to which they are attached, form a cycloalkyl group or a heterocycloalkyl group;

 R_7 is H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, $-OR_{17}$, $-SR_{17}$, $-NR_{17}R_{18}$, $-NR_{19}NR_{17}R_{18}$, or $-NR_{17}OR_{18}$, wherein R_{17} , R_{18} , and R_{19} independently are H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, or an acyl group;

or R_7 , together with R_3 or R_6 and the atoms to which they are attached, forms a heterocycloalkyl group;

R₂₀ is H, OH, or any suitable organic moiety; and

Z and Z_1 are independently H, F, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, $-C(O)R_{21}$, $-CO_2R_{21}$, -CN, $-C(O)NR_{21}$, R_{22} , $-C(O)NR_{21}OR_{22}$, $-C(S)R_{21}$, $-C(S)NR_{21}R_{22}$, $-NO_2$, $-SOR_{21}$, $-SO_2R_{21}$, $-SO_2NR_{21}R_{22}$, $-SO(NR_{21})(OR_{22})$, $-SONR_{21}$, $-SO_3R_{21}$, $-PO(OR_{21})_2$, $-PO(R_{21})(R_{22})$, $-PO(NR_{21}R_{22})(OR_{23})$, $PO(NR_{21}R_{22})(NR_{23}R_{24})$, $-C(O)NR_{21}NR_{22}R_{23}$, or $-C(S)NR_{21}NR_{22}R_{23}$,

wherein R_{21} , R_{22} , R_{23} , and R_{24} are independently H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, an acyl group, or a thioacyl group, or wherein any two of R_{21} , R_{22} , R_{23} , and R_{24} , together with the atom(s) to which they are bonded, form a heterocycloalkyl group;

or Z_1 , as defined above, together with R_1 , as defined above, and the atoms to which Z_1 and R_1 are bonded, form a cycloalkyl or heterocycloalkyl group,

or Z and Z_1 , both as defined above, together with the atoms to which they are

bonded, form a cycloalkyl or heterocycloalkyl group;
or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate
thereof;

and wherein said compound, or pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof, has antipicornaviral activity with an EC $_{50}$ less than or equal to 10 μ M in the HI-HeLa cell culture assay.

- 2. At least one compound of claim 1, wherein R_1 is H or F, or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.
- 3. At least one compound of claim 1, wherein R_{20} is H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, OR_{17} , - SR_{17} , - $NR_{17}R_{18}$, - $NR_{19}NR_{17}R_{18}$, or - $NR_{17}OR_{18}$, wherein R_{17} , R_{18} , and R_{19} independently are H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, or an acyl group, or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.
- 4. At least one compound of claim 3, wherein R_{20} is the alkyl group $C(R_{41})(R_{42})NR_{43}R_{44}$, wherein:

R₄₁ and R₄₂ independently are H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group; and R₄₃ and R₄₄ independently are H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, -NR₄₅R₄₆, -C(O)R₄₅, -C(S)R₄₅, -C(O)NR₄₅R₄₆, -C(S)NR₄₅R₄₆, -C(O)NR₄₅OR₄₆, -C(S)NR₄₅OR₄₆, -C(S)NR₄₅OR₄₆, -C(S)NR₄₅OR₄₆, -C(S)NR₄₅OR₄₅, -C(S)SR₄₅, -OR₄₅, -SR₄₅, -C(O)NR₄₅NR₄₆R₄₇, -C(S)NR₄₅NR₄₆R₄₇, -SOR₄₅, -SO₂R₄₅, -S(O)NR₄₅R₄₆, -S(O)NR₄₅(OR₄₆), -SO₂NR₄₅R₄₆, -SO₂NR₄₅(OR₄₆), or -SO₃R₄₅,

wherein R₄₅, R₄₆, and R₄₇ independently are H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group,

or wherein any suitable combination of R₄₁, R₄₂, R₄₃, and R₄₄ together form a cycloalkyl group or a heterocycloalkyl group;

or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.

- 5. At least one compound of claim 4, wherein at least one of R_{43} or R_{44} is $-C(O)SR_{45}$ or $-C(O)OR_{45}$, or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.
- 6. At least one compound of claim 5, wherein R₄₅ is an alkyl group, a cycloalkyl group, an aryl group, a heterocycloalkyl group, or a heteroaryl group, or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.
- 7. At least one compound of claim 6, wherein R₄₅ is a C₁-C₁₀ alkyl group or a cycloalkyl group, or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.
- 8. At least one compound of claim 1, wherein at least one of R_2 or R_5 is

$$X$$
 Y_1
 A_1
 D_1

or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.

9. At least one compound according to claim 8, wherein D_1 is $-OR_{25}$, =O, =S, $\equiv N$, $=NR_{25}$, or $-NR_{25}R_{26}$, wherein R_{25} and R_{26} are independently H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group, or, together with the nitrogen atom to which they are bonded, form a

heterocycloalkyl group; or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.

- 10. At least one compound according to claim 9, wherein D_1 is =0; or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.
- 11. At least one compound according to claim 8, wherein A₁ is C, CH, S, or S(O); or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.
- 12. At least one compound according to claim 11, wherein A_1 is C; or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.
- 13. At least one compound according to claim 8, wherein B_1 is $NR_{17}R_{18}$, wherein R_{17} and R_{18} are independently H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, an acyl group; or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.
- 14. At least one compound according to claim 1, wherein at least one of R_2 or R_5

or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.

15. At least one compound according to claim 14, wherein D_2 is $-OR_{25}$, =O, =S, $\equiv N$, $=NR_{25}$, or $-NR_{25}R_{26}$, wherein R_{25} and R_{26} are independently H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group, or, together with the atom(s) to which they are bonded, form a heterocycloalkyl group; or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.

- 16. At least one compound according to claim 15, wherein D_2 is =0; or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.
- 17. At least one compound according to claim 14, wherein A_2 is C, CH, S, or S(O); or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.
- 18. At least one compound according to claim 17, wherein A_2 is C; or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.
- 19. At least one compound according to claim 14, wherein B_2 is -NR₁₇R₁₈, wherein R_{17} and R_{18} are independently H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, an acyl group; or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.
- 20. At least one compound according to claim 1, wherein A_1 is C, CH, S, or S(O) or wherein A_2 is C, CH, S, or S(O); or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.
- 21. At least one compound according to claim 1, wherein Z and Z_1 are independently H, an aryl group, or a heteroaryl group, $-C(O)R_{21}$, $-CO_2R_{21}$, -CN, $-C(O)NR_{21}R_{22}$, $-C(O)NR_{21}OR_{22}$, $-C(S)R_{21}$, $-C(S)NR_{21}R_{22}$, $-NO_2$, $-SOR_{21}$, $-SO_2R_{21}$, $-SO_2NR_{21}R_{22}$, $-SO(NR_{21})(OR_{22})$, $-SONR_{21}$, $-SO_3R_{21}$, $-C(O)NR_{21}NR_{22}R_{23}$, or $-C(S)NR_{21}NR_{22}R_{23}$;

wherein R_{21} , R_{22} , and R_{23} are independently H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, an acyl group, or a thioacyl group, or wherein any two of R_{21} , R_{22} , and R_{23} , together with the atom(s) to which they are bonded, form a heterocycloalkyl group;

or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.

- 22. At least one compound according to claim 1, wherein M is O.
- 23. At least one compound having the formula X:

$$R_{66}$$
 R_{64}
 R_{63}
 R_{67}
 R_{61}
 R_{61}
 R_{62}
 R_{62}
 R_{63}
 R_{67}
 R_{61}
 R_{61}
 R_{62}
 R_{63}
 R_{64}
 R_{65}
 R_{65}

wherein

R₆₁ is H, F, or an alkyl group;

R₆₂ is selected from one of the following moieties:

wherein

R₃₅ is H, an alkyl group, an aryl group, -OR₃₈, or -NR₃₈R₃₉,

wherein R₃₈ and R₃₉ independently are H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, or an acyl group; and

R₃₆ is H or an alkyl group,

or R₃₅ and R₃₆, together with the nitrogen atom to which they are attached,

form a heterocycloalkyl group or a heteroaryl group;

 R_{37} is an alkyl group, an aryl group, or -NR₃₈R₃₉, wherein R₃₈ and R₃₉ are as defined above;

 R_{50} is H, an alkyl group, an aryl group, $-OR_{38}$, $-SR_{39}$, $-NR_{38}R_{39}$, $-NR_{40}NR_{38}R_{39}$, or

-NR₃₈OR₃₉, or R₅₀ and R₃₆, together with the atoms to which they are attached, form a heterocycloalkyl group;

wherein R_{38} and R_{39} are as defined above, and R_{40} is H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, or an acyl group; and

n is 0, 1, or 2;

R₆₃ is H or an alkyl group;

R₆₄ is H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group;

 R_{65} is H or an alkyl group;

R₆₆ is H, an acyl group, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a sulfonyl group, or a heteroaryl group;

R₆₇ is H or an alkyl group;

and

Z and Z_1 are independently H, F, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, $-C(O)R_{21}$, $-CO_2R_{21}$, -CN, $-C(O)NR_{21}R_{22}$, $-C(O)NR_{21}OR_{22}$, $-C(S)R_{21}$, $-C(S)NR_{21}R_{22}$, $-NO_2$, $-SOR_{21}$, $-SO_2R_{21}$, $-SO_2NR_{21}R_{22}$, $-SO(NR_{21})(OR_{22})$, $-SONR_{21}$, $-SO_3R_{21}$, $-PO(OR_{21})_2$, $-PO(R_{21})(R_{22})$, $-PO(NR_{21}R_{22})(OR_{23})$, $-PO(NR_{21}R_{22})(NR_{23}R_{24})$, $-PO(NR_{21}R_{22})$

 $C(O)NR_{21}NR_{22}R_{23}$, or $-C(S)NR_{21}NR_{22}R_{23}$,

wherein R_{21} , R_{22} , R_{23} , and R_{24} are independently H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, an acyl group, or a thioacyl group, or wherein any two of R_{21} , R_{22} , R_{23} , and R_{24} , together with the atom(s) to which they are bonded, form a heterocycloalkyl group,

or Z and Z_1 , both as defined above, together with the atoms to which they are bonded, form a heterocycloalkyl group;

or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.

- 24. At least one compound according to claim 23, wherein R_{66} is the acyl group -C(O)OR₆₈ or the acyl group -C(O)SR₆₈, wherein R₆₈ is an alkyl group, a cycloalkyl group, an aryl group, a heterocycloalkyl group, or a heteroaryl group, or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.
- 25. At least one compound according to claim 4, having the formula II:

wherein R_1 , R_5 , R_6 , R_7 , R_{42} , R_{43} , and Z are H, R_2 is $CH_2CH_2C(O)NH_2$, and R_3 is CH_2Ph , R_{41} is $CH_2CH(CH_3)_2$, Z_1 is $CO_2CH_2CH_3$, and R_{44} is

R₃ is CH₂Ph, R₄₁ is CH₂CH(CH₃)₂, Z₁ is CO₂CH₂CH₃, and R₄₄ is

attates !

$$R_3$$
 is CH_2Ph , R_{41} is $CH_2CH(CH_3)_2$, Z_1 is , and R_{44} is

 R_3 is CH_2Ph , R_{41} is $CH(CH_3)_2$, Z_1 is $CO_2CH_2CH_3$, and R_{44} is CH_2CH_3

 R_3 is CH_2Ph , R_{41} is $CH(CH_3)_2$, Z_1 is $CO_2CH_2CH_3$, and R_{44} is

R₃ is CH₂Ph, R₄₁ is CH₂CH(CH₃)₂, Z₁ is CO₂CH₂CH₃, and R₄₄ is

R₃ is CH₂Ph, R₄₁ is CH(CH₃)₂, Z₁ is CO₂CH₂CH₃, and R₄₄ is

R₃ is CH₂Ph, R₄₁ is CH₂CH(CH₃)₂, Z₁ is CO₂CH₂CH₃, and R₄₄ is

$$Q_{s}$$

R₃ is $CH_2(p-CH_3)Ph$, R_{41} is $CH(CH_3)_2$, Z_1 is $CO_2CH_2CH_3$, and R_{44} is CH_3CH_2S or

 R_3 is $CH_2(p\text{-}CH_3)Ph$, R_{41} is $CH(CH_3)_2$, Z_1 is $CO_2CH_2CH_3$, and R_{44} is

or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.

26. At least one compound according to claim 4, having the formula III:

wherein R_1 , R_5 , R_6 , R_7 , R_{42} , R_{43} , and Z are H, R_3 is CH_2Ph , R_2 is $CH_2CH_2C(O)NH_2$,

R₄₁ is CH₂CH(CH₃)₂, Z₁ is CO₂CH₂CH₃, and R₄₄ is or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.

27. At least one compound of the formula (IV):

wherein:

 R_1 , R_5 , R_6 , R_7 , and R_{42} are H, R_2 is $CH_2CH_2C(O)NH_2$, and R_3 is $CH_2(p\text{-}CH_3)Ph$, Z is H, Z_1 is $CO_2CH_2CH_3$, R_{41} is CH_2Ph , and R_{44} is

 R_3 is $CH_2(p-F)Ph$, Z is H, Z_1 is $CO_2CH_2CH_3$, R_{41} is $CH(CH_3)_2$, and R_{44} is CH_3CH_2S

 R_3 is $CH_2(p-F)Ph$, Z is H, Z_1 is $CO_2CH_2CH_3$, R_{41} is $CH(CH_3)_2$, and R_{44} is

 R_3 is $CH_2(p\text{-}CF_3)Ph$, Z is H, Z_1 is $CO_2CH_2CH_3$, R_{41} is $CH(CH_3)_2$, and R_{44} is CH_3

 R_3 is $CH_2(p\text{-}CF_3)Ph$, Z is H, Z_1 is $CO_2CH_2CH_3$, R_{41} is $CH(CH_3)_2$, and R_{44}

 R_3 is $CH_2(p\text{-}CH_3)Ph$, Z and Z_1 together form (where * indicates the point of attachment and the carbonyl group is cis to the R_1 group), R_{41} is

 R_3 is $CH_2(p-F)Ph$, Z is H, Z_1 is $CO_2CH_2CH_3$, R_{41} is CH_2Ph , and R_{44} is

 R_3 is $CH_2(p-F)Ph$, Z is H, Z_1 is $CO_2CH_2CH_3$, R_{41} is $CH_2CH(CH_3)_2$, and

 R_3 is $CH_2(p\text{-}CH_3)Ph$, Z is H, Z_1 is $CO_2CH_2CH_3$, R_{41} is $CH(CH_3)_2$, and R_{44} is

 R_3 is $CH_2(p\text{-}CH_3)Ph$, Z is H, Z_1 is $CO_2CH_2CH_3$, R_{41} is $CH_2CH(CH_3)_2$, and R_{44} is

R₃ is CH₂Ph, Z is H, Z₁ is CO₂CH₂CH₃, R₄₁ is C(CH₃)₃, and R₄₄ is

 R_3 is $CH_2(p-CH_3)Ph$, Z is H, Z_1 is $CO_2CH_2CH_3$, R_{41} is $CH(CH_3)_2$, and R_{44}

R₃ is CH₂(p-F)Ph, Z is H, Z₁ is CO₂CH₂CH₃, R₄₁ is cyclohexyl, and R₄₄ is

R₃ is CH₂(p-F)Ph, Z is H, Z₁ is CO₂CH₂CH₃, R₄₁ is CH(CH₃)₂, and R₄₄ is

or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.

28. A composition comprising at least one compound of formula II:

wherein R_1 , R_5 , R_6 , R_7 , R_{42} , R_{43} , and Z are H, R_3 is CH_2Ph , R_2 is $CH_2CH_2C(O)NH_2$,

$$R_{41}$$
 is $CH_2CH(CH_3)_2$, Z_1 is $CO_2CH_2CH_3$, and R_{44} is

or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof,

and at least one compound of formula III:

$$R_{44}$$
 R_{43}
 R_{6}
 R_{6}
 R_{7}
 R_{7}
 R_{1}
 R_{1}
 R_{1}
 R_{1}
 R_{2}
 R_{1}
 R_{2}
 R_{1}
 R_{2}
 R_{1}
 R_{2}
 R_{1}
 R_{2}
 R_{1}
 R_{2}
 R_{2}
 R_{2}
 R_{2}
 R_{2}
 R_{3}
 R_{4}
 $R_$

wherein R_1 , R_5 , R_6 , R_7 , R_{42} , R_{43} , and Z are H, R_3 is CH_2Ph , R_2 is $CH_2CH_2C(O)NH_2$,

R₄₁ is CH₂CH(CH₃)₂, Z₁ is CO₂CH₂CH₃, and R₄₄ is or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.

- 29. A pharmaceutical composition comprising:
- (a) a therapeutically effective amount of at least one compound as defined in claim 1 or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof; and
- (b) a pharmaceutically acceptable carrier, diluent, vehicle, or excipient.
- 30. A method of treating a mammalian disease condition mediated by picornaviral protease activity that comprises administering to a mammal in need thereof a therapeutically effective amount of at least one compound as defined in claim 1 or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.
- 31. A method of inhibiting the activity of a picornaviral 3C protease that comprises contacting the picornaviral 3C protease with an effective amount of at

least one compound as defined in claim 1 or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.

- 32. A method of inhibiting the activity of a rhinoviral protease that comprises contacting the rhinoviral protease with an effective amount of at least one compound as defined in claim 1 or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof.
- 33. A compound according to claim 1, or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof, wherein said antipicornaviral activity is antirhinoviral activity.
- 34. A compound according to claim 1, or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof, wherein said antipicornaviral activity is anticoxsackieviral activity.